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14. ABSTRACT

The goal of our research program is to construct an electronic olfactory system (enose) that has the sensitivity, intelligence and discriminative capability of the mammalian olfactory system, as exemplified by a trained sniffer dog. We aim to create both the sensor array front end and the pattern analysis and learning back end. Our criteria for success include rapid and reliable detection of trace gas signals from both humans and ordinance.
We have developed a novel sensor technology based on DNA-decorated single-walled semiconducting carbon nanotubes arrayed as semiconductor elements in field effect transistors. We have greatly expanded the set of DNA sequences tested for odorant reactivity and the set of volatile organic compounds tested for sensor activation. We designed and fabricated a 50-sensor chip with a "crossbar" addressing scheme that scales to thousands of devices. We have also designed and constructed key electronic components for a 50 sensor chip, as an important milestone on our path to making multi-sensor measurements from an array of sensors with differing response profiles to a range of odorants found in human odor signatures. We have established that the

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Super-Sensing of Human and Environmental Odors

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The goal of our research program is to construct an electronic olfactory system (enose) that has the sensitivity, intelligence and discriminative capability of the mammalian olfactory system, as exemplified by a trained sniffer dog. We aim to create both the sensor array front end and the pattern analysis and learning back end. Our criteria for success include rapid and reliable detection of trace gas signals from both humans and ordinance.

We have developed a novel sensor technology based on DNA-decorated single-walled semiconducting carbon nanotubes arrayed as the semiconductor elements in field effect transistors (Gelperin and Johnson, 2008; Johnson et al., 2009). A diagram of our sensor is shown in Figure 1. Our strategy is to broaden and deepen our understanding of the ability of this new sensor technology to respond to and discriminate between odorants while simultaneously developing the pattern recognition and machine learning techniques to process sensor array data. Our progress in these areas will be presented in three parts dealing with sensor development, odor sampling with a commercial sensor array, and algorithm development.

Sensor Development

In this reporting period, we have expanded the set of nucleotide sequences and the set of odors tested for sensor responsiveness. To date we have tested 15 DNA sequences and 17 volatile organic compounds (VOCs), although not all possible combinations have been tested (see Table included with this report). The results clearly demonstrate that a diverse set of odor responses can be obtained by varying the base sequence and base composition of the DNA decorating the carbon nanotube. The results support the view that the range and diversity of odor responses available with this new sensor technology is adequate to the task of making a large sensor array capable of producing an information-rich pattern of response to real-world odor objects to allow rapid and reliable identification of complex human odor signatures or trace amounts of drug or ordinance odors.

The original panel of odorants we used is comprised of propionic acid (PA), trimethylamine (TMA), methanol (ME), 2,6, dinitrotoluene (DNT), and dimethyl methylphosphonate (DMMP), to allow direct comparison with sensor responses of DNA films (White et al., 2008). In subsequent work we have used twelve additional odorants and examined responses to thirteen new base sequences in addition to the original two sequences in our published work, as shown in Tables appended to this report.

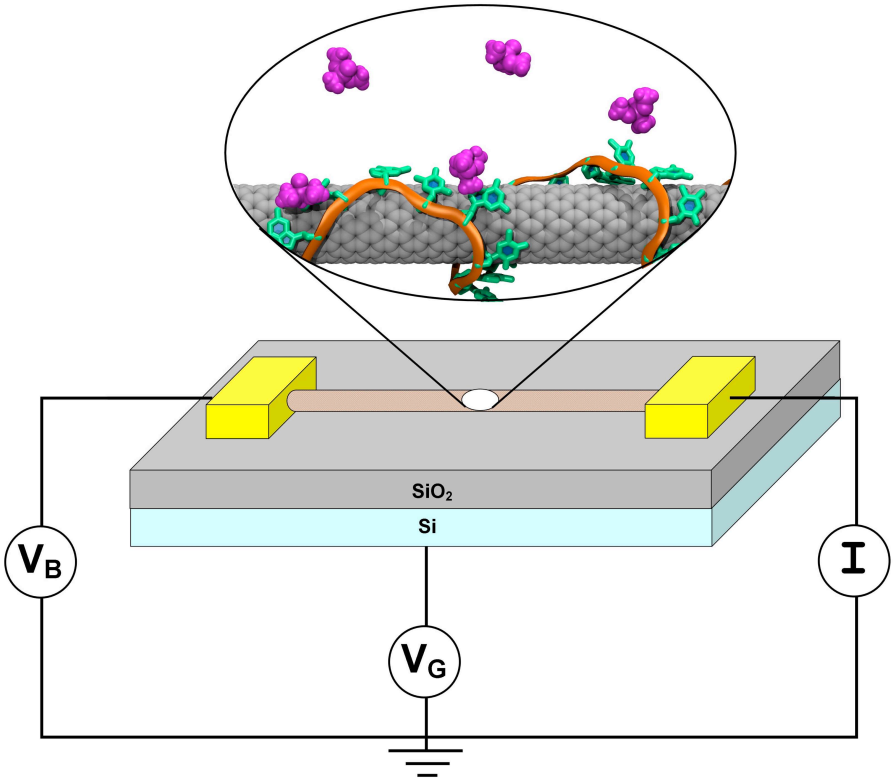

Figure 1 A semiconducting single-walled carbon nanotube is arrayed between source and drain electrodes with an imposed gate voltage (V_G) and source-drain voltage (V_B). Source-drain current (I) is measured while pulses of odorants are applied to the DNA-coated carbon nanotube.

We have accomplished the following milestones during the period covered by this report:

- We have designed and fabricated a 50-sensor chip with a “crossbar” addressing scheme that scales to thousands of devices. We have also designed and constructed key electronic components for a 50 sensor chip, as an important milestone on our path to making multi-sensor measurements from an array of sensors with differing response profiles to a range of odorants found in human odor signatures.

- We have established that the DNA/NT sensor class is capable of remarkable chemical differentiation between chemical homologues, structural isomers, and even stereoisomers (Figure 2). To our knowledge, this level of chemical differentiation, which is a common attribute of biological olfaction, has never been reported for an artificial vapor sensor.

- We have demonstrated that the DNA/NT sensor class is sensitive to volatile biomarkers of human melanoma, specifically dimethylsulfone at a biologically relevant concentration of 25 ppb. We have also demonstrated that DNA/NT sensors are capable of distinguishing between the volatile head space components characteristic of in vitro samples of normal melanocytes, and melanoma cells of various types.

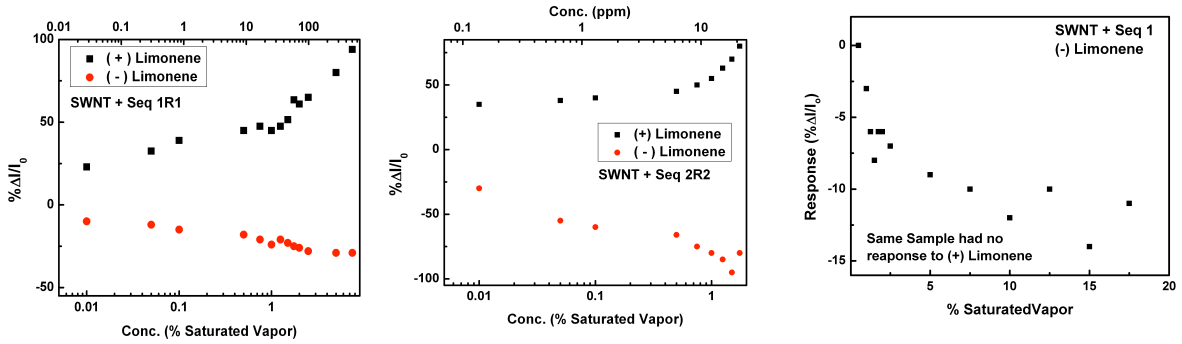

Figure 2 Responses of a small set of sensor devices coated with a given DNA oligomer (Seq1R1, Seq 2R2, and Seq 1, respectively) to application of various concentrations of (-) and (+) Limonene.

- We have licensed several patent filings connected to the DNA/NT vapor sensor to a startup company, Nanosense, Inc., that will produce an electronic nose system based on this sensor platform and a novel neurally inspired signal processing system. A Penn Ph.D. student and an undergraduate student from Johnson's lab (Dr. Samuel Khamis and Mr. Ryan Jones) are Nanosense's first employees. Nanosense has designed and fabricated an array of 1600 NT devices. Thus this technology is on a rapid path to commercialization. The Penn/Monell team is in close communication with Nanosense, and we plan a research program focused on fundamental scientific issues that arise in the design and optimization of the sensor array.

- We have developed a process for CVD growth of large area (inch scale) graphene films that can then be transferred to arbitrary substrates. Most recently, we discovered that the growth is optimized when the catalytic copper substrate is very smooth (polished) and the concentration of carbon feedstock gas (methane, in our case) is very low, resulting in graphene films that are over 95% single layer (manuscript submitted). Raman spectra are commonly used to assess the quality of graphene films (see Fig. 3). The key spectral features are the D (disorder) band at ~1350/cm, the G-band at ~1583/cm with a D' sideband at ~1620/cm, and the 2D band at ~2670/cm. The signatures of high quality graphene are i) very small D band intensity, ii) no trace of a D' sideband, and iii) a large 2D-to-G intensity ratio (I_{2D}/I_G>2). From the Raman spectra in Figure 3 we conclude that the use of polished Cu substrates and lower methane concentration are both associated with improved quality of the synthesized graphene. Electron transport measurements show that the carrier mobility of the graphene is

improved by a factor of 5-10. A manuscript reporting this advance in graphene synthesis has been submitted for publication in the Journal of the American Chemical Society. Support from this grant was cited.

Our intention is to explore the possibility of substituting CVD graphene for the nanotube component of our sensor system. Graphene, a single layer of graphite, is a zero-gap semiconductor, with excellent sensing characteristics similar to those of semiconducting nanotubes. We have published data showing that a graphene-based sensor device gave clear responses to 100 ppb octanoic acid vapor. We have also demonstrated that small pieces of single-layer graphene can make effective odor sensors after coating with DNA (submitted). Graphene devices are expected to have enhanced reproducibility compared to nanotube devices, since the latter require special processing to remove undesired metallic nanotubes, which show no sensor response.

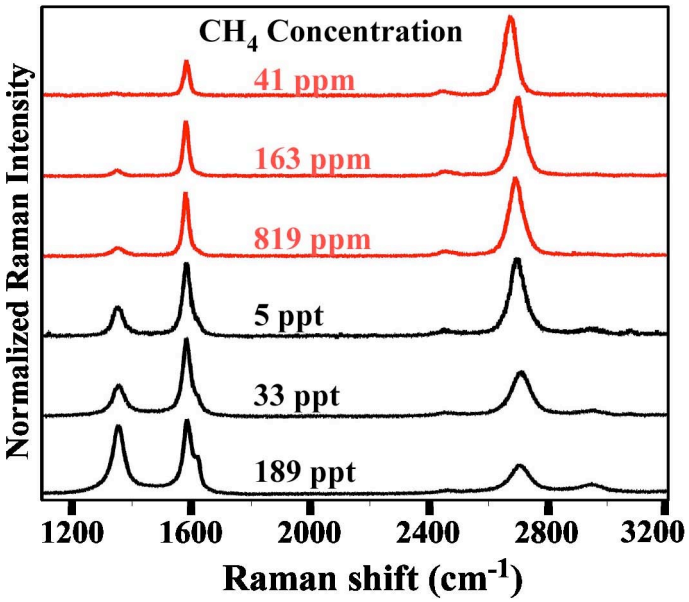

FIG. 3. Raman spectra of CVD graphene grown on as-obtained Cu foil (black data) and electropolished foil (red data) and then transferred to an oxidized silicon substrate. Raman spectra of graphene grown on unpolished and electropolished Cu foil were depicted in black and red curves, respectively.

Recent publications citing support from this grant;

1. Johnson AT, Khamis SM, Preti G, Kwak J, Gelperin A (2010) DNA-coated nanosensors for breath analysis. IEEE Sensors Journal 10:159-166.
2. Gelperin A (2010) Human olfactory perception. In: Chemistry and Biology of Volatiles (Herrmann A, ed), New York: John Wiley, in press.
3. Gelperin A, Ghatpande A (2009) Neural basis of olfactory perception. Ann N Y Acad Sci 1170:277-285.

4. Zhengtang Luo, Ye Lu, Daniel W. Singer, Matthew E. Berck, Luke A. Somers, Brett R. Goldsmith, A.T. Charlie Johnson (2010), Growth of uniform wafer-size graphene on electropolished copper, J. Am. Chem. Soc., in review.

Additional references;

1. Gelperin A, Johnson ATC (2008) Nanotube-based sensor arrays for clinical breath analysis. J Breath Research 2:#037015 (037016pp).
2. White J, Truesdell K, Williams LB, Atkisson MS, Kauer JS (2008) Solid-state, dye-labeled DNA detects volatile compounds in the vapor phase. PLoS Biol 6:e9.

All Measurements Performed at 3% Saturated Vapor Pressure

- Detectable at Higher Concentration
- Quoted values represent average of 5-20 measured devices

	Bare	Seq1	Seq1 α	Seq1 RNA	Seq1R1	Seq2	Seq2α	Seq 2 Soup	Seq2R1	Seq2R2	Seq2 RNA	GT_{12}	A_{21}	C_{21}	G_{21}	T_{21}
Propionic Acid	0±1	+17±2	0±1	+45 ± 10		+8±1	+10±3	0±1			+40 ± 5	0±1	0 ±1	0 ±1	0 ±1	0 ±1
Hexanoic Acid		0±4 *														
Octanoic Acid		0±4 *														
2-Methyl Valeric Acid	3±2	35±7				5±3										
4-Methyl Valeric Acid	0±3	30±5				12±4										
n-Octanal		-50±5														
n-Nonanal		-13 ± 5														
n-Decanal		0±4 *														
DMMP	0±1	-14±2	0±1	+30 ± 5		-7±2	-15±2	0±1			-35 ± 10	0 ±1	0 ±1	0 ±1	0 ±1	0 ±1
DNT	0±1	-14±4	0±1	-20 ± 5		-4±2	0±4	0±1			-70 ± 10	0 ±1	0 ±1	0 ±1	0 ±1	0 ±1
(+) Limonene	5±2	13±4			50±7	40±8			80±8	60±8						
(-) Limonene	-7±3	-7±4			-30±5	6±3			-65±9	-80±10						
L-Carvone	-7±4	-20±5				-10±4										
D-Carvone	-8±4	-10±5				-15±5										
Methanol	0±1	-12±2	-50±2	32 ± 5		-20±2	8±1	-60±4			20 ± 5	-4 ±2	-15 ±2	0 ±1	-50 ±2	0 ±1
Trimethylamine	-9±2	-20±2	-20±3	-40 ± 10		-30±2	14±2	-25±5			-45 ± 5	-50 ±5	-25 ±3	-16 ±5	-50 ±6	-10 ±6
Dimethyl sulfone (500ppm)		50±10														

Bare SWNT	
Seq1	GAGTCTGTGGAGGAGGTAGTC
Seq1 α	AAAACCGGGGGGGGGGTTTTT
Seq 1 RNA	GAGUCUGUGGAGGAGGUAGUC
Seq 1R1	CGAGGGAGTTGTACTTGGAGG
Seq 1R2	TGATGTGGGTGCCGAAGGTGA
Seq 2	CTTCTGTCTTGATGTTTGTCAAAC
Seq 2 α	AAAACCCCCGGGGTTTTTTTTTTT
Seq 2 Soup	4dATP : 5dCTP : 4dGTP : 11dTTP
Seq2 RNA	CUUCUGUCUUGAUGUUUGUCAAAC
Seq 2R1	TACTGTCTCATTCTGGATATTCTG
Seq 2R2	GAATATGTACTTGTCCCTGTTCTT
GT_{12}	GTGTGTGTGTGTGTGTGTGTGT
A_{21}	AAAAAAAAAAAAAAAAAAAAA
C_{21}	CCCCCCCCCCCCCCCCCCCCC
G_{21}	GGGGGGGGGGGGGGGGGGGGG
T_{21}	TTTTTTTTTTTTTTTTTTTTT